Free Associations: Psychoanalysis and Culture, Media, Groups, Politics
Number 74 December 2018 ISSN: 2047-0622
URL: http://www.freeassociations.org.uk/

Biogenetic Overreach

by Steve Pittelli

Blueprint: How DNA Makes Us What We Are (MIT Press, 2018) is the latest book by genetics researcher and author, Robert Plomin. It begins with discussions about twin and adoption studies, an area where Dr. Plomin has extensive experience as a researcher. This serves as a springboard for Plomin to discuss DNA research, particularly "polygenic scores," for which he possesses an almost evangelical zeal. Mixing this with his own research anecdotes and theories about a self-described "DNA Revolution," Plomin's meandering narrative is, at times, difficult to follow and has a utopian feel.

As Plomin acknowledges, much of the early DNA research related to psychological traits (and most traits in general) failed to find specific genes related to the trait in question. When such genes were found, the experiments were never replicated, creating a "replication crisis" in the field. In Dr. Plomin's view, this crisis was solved by the larger datasets now available and the polygenic score, which "predicts" the likelihood of particular traits by tallying up the number of genetic variants a person has that have been shown to correspond in some way to particular traits. I would suggest that this is a significant lowering of the bar for replication and does not eliminate the crisis.

Throughout, Plomin presents theories about genetics and psychological traits, some being current paradigms in the field, such as "polygenic inheritance," and some being his own ideas, adding some of his own terms ("generalist genes," "non-shared environment"). He makes little distinction between these theories and generally presents all of it as proven fact, providing limited evidence other than the above-noted twin and adoption studies. This style finds him occasionally wrestling with contradictions. The first involves an issue of the nature versus nurture argument. He notes that 50% of particular behavioral traits should be attributable to genetics based on twin studies, but largely negates specific environmental factors as contributors, noting that parents, schools and life experiences "don't make a difference," leaving us with the question of the other 50%. This is compounded by the fact that siblings sharing 50% of the same DNA, are often very different. He chalks this up to unnamed, "non-shared environment," guided by "...unsystematic, idiosyncratic, serendipitous events with lasting effects." Whether conscious or unconscious, such an explanation is not entirely different from mystical or supernatural explanations.

Since Dr. Plomin is unable to define these non-shared environmental factors, and they don't fit into his "blueprint" ideology, he largely dismisses them and focuses on the other 50% as if it were 100%, which leads him to use polygenic scores as a way of defining almost any trait. He makes his case through examples such as height and weight, which one would expect to have a relatively normal (bell curve) distribution, equating their distribution with the bell curve distribution seen for polygenic scores for these traits. Using physical traits like these as your model for something as dynamic and complex as psychological traits, such as schizophrenia, is perhaps dubious, but Plomin doubles down on this and states that schizophrenia can no longer be considered as an either/or

diagnosis, but must be viewed as a continuum, largely because it otherwise would not fit his theory.

Thus, it's a matter of how many schizophrenic genetic variants someone has, with only those at the extreme end currently receiving the diagnosis. "Who has not sometimes experienced these symptoms [hallucinations, delusions, disorganized thoughts, etc.]," he asks? This would imply that, in addition to those we diagnose with schizophrenia, there is a larger population of somewhat schizophrenic individuals, an even larger population being a little bit schizophrenic and another half of the bell curve for those with gradations of "un-schizophrenia." As a psychiatrist, I treated schizophrenia for many years and find this notion absurd. No psychiatric diagnosis is perfect, but schizophrenia is a relatively distinct diagnosis, as are most other psychiatric diagnoses. They do not tend to fall into a bell curve continuum. Thus, it appears that Plomin embraces his theory at the expense of reality. His claim that, "psychiatric diagnoses are not supported by genetic research," does not lead him to question the validity of the genetic research. Instead, he proposes scrapping current diagnostic criteria, asserting that, "Genetics offers a causal basis for predicting disorders, rather than waiting for symptoms to appear." This strikes me as science fiction.

Plomin continues in this vein, promulgating a "DNA Revolution" view of society at large, specifically focusing on "educational achievement," a trait for which a recent DNA study has been performed with polygenic score results that claim 11% predictability. He accepts the accuracy of this and presumably expects that it will inevitably approach 100%, even suggesting that elite school selection be based on "inherited DNA differences." To his credit, Plomin addresses economic inequality and social mobility, concerns related to these genetic-based decisions, even suggesting that his genetic model will improve them. However, the difficulties he has juggling this with his belief that genetics are the primary basis for educational achievement are obvious. For example, he suggests that some social mobility would occur due to the variance in educational achievement within families (back to the mystical, "non-shared environment"), allowing some to move up and others to move down. Plomin overlooks the point that, within an educational landscape where opportunities are determined by profiling of inherited DNA, individuals who are more able due to non-shared environment would not have the opportunity to advance. Conversely, those less able from a privileged family would not move down since they have the preferred DNA.

Plomin also addresses the concern that such a society would lead to the creation of a kind of DNA caste system wherein those possessing auspicious DNA would isolate themselves and stratify society based on DNA. This, argues Dr. Plomin, would not likely happen. However, his argument is a convoluted extension of the non-shared environment idea and assumes mating patterns that are blind to the DNA of partners. The idea that a potential mate's specific DNA would not be a primary factor in such a system is hard to entertain. I would argue that even without knowing the specific DNA of others, we already have DNA castes, to some extent. People tend to marry, whether naturally or in a planned way, within their own race and social groups. While there is certainly more mixing than one would find in the caste system of India, that would likely change when one realizes that the DNA of our partner would be a factor in the opportunities for our

children, whether or not the DNA has anything to do with their ability. To suggest otherwise is rather naïve and unrealistic.

Also confusing is Plomin's statement that polygenic scores are causal. I know of no other reputable geneticist who makes such a claim. He writes, "Predictions from polygenic scores are an exception to the rule that correlations do not imply causation," and attributes an almost life-like quality to these statistical scores. Causation implies that the correlation is directly related to the trait. Even Dr. Plomin admits that at least some of the genetic variants used in a polygenic score are "false positives." As yet, in fact, no specific genetic variant used in a polygenic score for any psychological trait has been clearly demonstrated to have a direct causal relationship to the trait in question. It is therefore a leap of faith to claim that polygenic scores are causal when we cannot even demonstrate that any of the genetic variants being used to create the score are causal.

This brings me to the potential problem of population stratification, which has confounded genetic studies as disparate as height, weight, socioeconomic status and schizophrenia, leading to false positive findings. Dr. Plomin doesn't address this to any extent and I think it would be a particular concern for something like educational achievement. Population stratification occurs when we have differences in allele frequencies in subpopulations closed in some way by geography or social/cultural reasons, giving the impression that variants common within the subpopulation are related to the trait being examined, when they are not. The same principle is used to advantage by companies like Ancestry.com to identify variants that stratify among a particular geographic or ethnic group.

As Plomin notes, for example, the small percentage of students attending private schools (in the U.K.) tend to have extremely disproportional representation amongst doctors, judges, top journalists, government officials, etc. This is a somewhat closed social group that marries within the group and has done so for generations. Plomin argues that parents will pass on their genes to their children, perpetuating families of genetically gifted individuals who we would expect to have greater educational achievement. However, one would also expect that the people in such a closed group would inevitably develop some genetic commonalities unrelated to educational achievement.

So, the question is to what extent these unrelated genetic markers will be flagged along with the presumed genes related to educational achievement, and appear as part of the polygenic score? Currently, we have very little idea what the genetic variants do and whether they have any direct relationship to educational attainment. This would give a currency of genetic variants to individuals, presumably in the elite social group, which may have nothing do with educational attainment and everything to do with being a part of that group. In effect, you could have a DNA aristocracy that is not actually related to any functions of that DNA. It's worth noting, in that regard, that the cited 11% predictability of the polygenic score for educational achievement cited by Plomin applies only to white, European individuals in the study. The score does not have the same predictability for other races.

In addition to the issue of stratification, there is also the question of accuracy. One of the more interesting and telling parts of the book is the N = 1 trial in which Dr.

Plomin shares some of his own polygenic scores for various traits. This starts off well, with his fairly high polygenic score for height matching the fact that he is tall. However, he also discovered that he had a high polygenic score for body mass index (BMI) and schizophrenia. Rather than just admit that these do not accurately reflect reality, Dr. Plomin justifies his inaccurately high BMI polygenic score, stating, "I came to accept that my high BMI polygenic score makes sense...[and] had a good effect on my attempts to persevere with my never ending battle of the bulge..." Similarly, related to his high polygenic score for schizophrenia, he notes, "...I wonder if my need for a highly structured, scheduled working life may be an attempt to keep myself on an even keel." Again, he values his theory over the reality in front of him. This kind of malleable self-assessment is reminiscent in tone to that of my "New Age" friends excitedly discussing their horoscopes.

Aside from creating more needless neurosis, it is hard to see the benefit of such polygenic scores. Dr. Plomin is old enough that he needn't worry about becoming schizophrenic or succumbing to a sudden large weight gain, but what if he, or anyone else, was presented with this inaccurate information as an adolescent? It could potentially alter the course of their lives in very negative ways. It would be irresponsible and potentially harmful to present this information to an individual as a factual "blueprint" for their future.

To conclude, there is little in this book that adds to what was already speculated related to twin and adoption studies of years past. Certainly, at this point, polygenic scores do not appear to be a reliable indicator of what traits or abilities a person will acquire, nor do they provide any explanation (as suggested in the book subtitle) as to the specific role any genes or variants play in creating a phenotype, if any. The theories Dr. Plomin provides related to his "DNA revolution," are inconsistent, and unrealistic. As a document of some of his life's work, this book might have some value, but it is otherwise lacking the substance needed to critically assess this kind of DNA research and misrepresents and exaggerates what we know to date.

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